THE EFFECTS OF ACUTE ETHANOL ON CHOLINERGIC ACTIVITY IN THE HIPPOCAMPUS AND NUCLEUS ACCUMBENS OF RAT BRAIN

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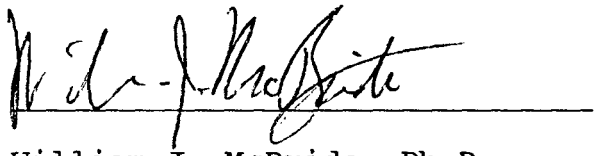
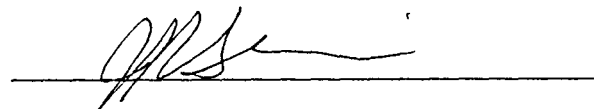


William J. McBride, Ph.D.



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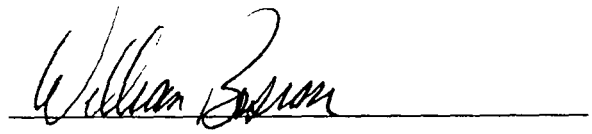

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ABSTRACT

The effects of *in vivo* administration of d-amphetamine (AMPH), pentylenetetrazole (PTZ) and ethanol on the *in vitro* measurements of high affinity choline uptake (HACU) into synaptosomes from the hippocampus (HIP) and nucleus accumbens (ACC) of rat brain were examined. Administration of 1.5 mg/kg AMPH increased the locomotor activity of rats 25-60 minutes following i.p. injection but did not alter HACU in the HIP or ACC 30 minutes after administration. PTZ injected i.p. increased HACU in the HIP and ACC by 31% and 18%, respectively, following the onset of the flexor stage of convulsions.

An initial study was conducted to demonstrate the *in vitro* technique of HACU as a method for measuring cholinergic activity *in vivo*. The effects of high potassium depolarization on subsequent measurements of high affinity (HA) choline, glutamate and GABA uptake were examined. A 45% increase in HACU after 62 mM K^+ depolarization was further characterized as an increase in V_{max}. HA glutamate and GABA uptake were unaffected by depolarizing concentrations of potassium. Kinetic analysis of HA glutamate uptake revealed no alteration in V_{max} or K_m. These results suggest that changes in

the HACU system are closely associated with changes in cholinergic neuronal activity, while alterations in neuronal activity of the amino acid systems do not produce changes in the HA uptake of glutamate or GABA.

Low dose ethanol (0.5 g/kg) produced blood alcohol concentrations (BAC's) less than 50 mg/dl, while the BAC's for high dose ethanol (2.5 g/kg) never exceeded 300 mg/dl. Compared to saline control values, high dose ethanol decreased HACU by 27% in the HIP and 24% in the ACC 60 minutes after administration. HACU was not significantly altered 15 minutes following high dose ethanol in either the HIP or ACC. Low dose ethanol did not significantly affect HACU 15 or 60 minutes following i.p. administration in either the HIP or ACC when compared with saline controls. Also, no locomotor stimulation was observed over 60 minutes in Wistar rats given low dose ethanol. These results suggest that ethanol affects central cholinergic systems in a dose and time dependent manner. Inhibition of cholinergic activity appears to occur with time at the high dose of ethanol. Central cholinergic systems respond differently to AMPH, PTZ and ethanol. Responses to these drugs in the HIP or ACC may be due to direct or indirect cholinergic involvement.

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